CLAIMS:

1. A compound of the general formula (II) and salts and physiologically functional derivatives thereof,

$$\begin{bmatrix} R^{1} \\ R^{2} \end{bmatrix}_{R} = \begin{bmatrix} D_{m} - \left(CHR^{3}\right)_{n} \end{bmatrix}_{q} - Y$$

wherein

5

10

25

A is a heteroaromatic 5-membered ring system containing one or more groups X selected from the group consisting of S, O, N, NR⁴, SO₂ and SO;

D is O, S, SO₂, NR⁴, or CH₂;

Z¹ and Z² are independent from each other O, S, or NR⁵;

independently represents H, halogen, haloalkyl, haloalkyloxy -CO₂R'', -SO₃H, -OH, -CONR*R'', -CR''O, -SO₂-NR*R'', -NO₂, -SO₂-R'', -SO-R*, -CN, alkoxy, alkylthio, aryl, -NR''-CO₂-R', -NR''-CO-R*, -NR''-SO₂-R', -O-CO-R*, -O-CO₂-R*, -O-CO-NR*R''; cycloalkyl, alkylamino, hydroxyalkylamino, -SH, heteroaryl, or alkyl;

20 R* independently represents H, alkyl, cycloalkyl, aminoalkyl, alkoxy, -OH, -SH, alkylthio, hydroxyalkyl, haloalkyl, haloalkyloxy, aryl or heteroaryl;

R' independently represents H, -CO₂R'', -CONHR'', -CR''O, -SO₂NR'', -NR''-CO-haloalkyl, -NO₂, -NR''-SO₂-haloalkyl, -NR''-SO₂-alkyl, -NR''-CO-alkyl, -CN, alkyl, cycloalkyl, aminoalkyl, alkylamino, alkoxy, -OH, -SH, alkylthio, hydroxyalkyl, hydroxyalkylamino, halogen, haloalkyl, haloalkyloxy, aryl, arylalkyl or heteroaryl;

	R"	independently represents hydrogen, haloalkyl, hydroxyalkyl, alkyl, cycloalkyl, aryl, heteroaryl or aminoalkyl;
5	R²	is H or OR ⁶ , NHR ⁷ , NR ⁷ OR ⁷ or R ² together with the nitrogen atom which is attached to R ⁸ form a 5 or 6 membered heteroyclic ring with the proviso that R ² is -[CH ₂] _s and R ⁸ is absent;
10	R ³	is H, alkyl, cycloalkyl, aryl, alkoxy, O-aryl; O-cycloalkyl, halogen, aminoalkyl, alkylamino, hydroxylamino, hydroxylalkyl, haloalkyloxy, heteroaryl, alkylthio, S-aryl; S-cycloalkyl, arylalkyl, or haloalkyl;
15	R ⁴	is H, alkyl, cycloalkyl, aryl or heteroaryl;
	R ⁵	is H, OH, alkoxy, O-aryl, alkyl or aryl;
	R ⁶	is H, alkyl, cycloalkyl, aryl, arylalkyl, heteroaryl, alkylaryl, alkoxyalkyl, acylmethyl, (acyloxy)alkyl, non-symmetrical (acyloxy)alkyldiester, or dialkylphosphate;
20	R ⁷	is H, OH, alkyl, aryl, alkoxy, O-aryl, cycloalkyl, or O-cycloalkyl;
	R ⁸	is hydrogen, or alkyl;
25	E	is an alkyl or cycloalkyl group or a monocyclic or polycyclic substituted or unsubstituted ring system which may contain one or more groups X and which contains at least one aromatic ring;
	Y	is hydrogen, halogen, haloalkyl, haloalkyloxy, alkyl, cycloalkyl, a monocyclic or polycyclic substituted or unsubstituted ring system which
30		may contain one or more groups X and which contains at least one aromatic ring or

$$\begin{array}{c|c}
 & 31 \\
 & 2^2 \\
 & NR^8 \longrightarrow E \\
 & R^2
\end{array}$$

n is 0 or 1;

p is 0 or 1;

q is 0 or 1;

s is 0 to 2; and

t is 0 to 3;

with the proviso that the following compounds are excluded:

10 compounds wherein ring A contains five atoms, $Z^1=Z^2=0$, and R^2 together with the nitrogen atom which is attached to R^8 forms a 5 membered heteroyclic ring with the proviso that R^2 is $-[CH_2]_6$, R^8 is absent and s is 0;

compounds wherein ring A contains three carbon atoms and two nitrogen atoms, $Z^1=Z^2=0$, and R^2 together with the nitrogen atom which is attached to R^8 form a 5 membered heteroyclic ring with the proviso that R^2 is $-[CH_2]_s$, R^8 is absent and s is 0;

4-[4-(naphthalin-2-yl) thiazol-2-ylaminocarbonyl]-furan-3-carboxylic acid; and 5-[4-(naphthalin-2-yl]thiazol-2-ylaminocarbonyl]-2H-[1,2,3]-triazole-4-carboxylic acid.

20

15

5

2. The compound according to claim 1, with the proviso that the following compounds are additionally excluded:

2-[4-(naphthalin-2-yl)thiazol-2-ylaminocarbonyl]thiophene-3-carboxylic acid;

3-[4-(naphthalin-2-yl)thiazol-2-ylaminocarbonyl]thiophene-2-carboxylic acid.

25

- 3. A pharmaceutical composition comprising a compound as defined in claim 1 in free form or in the form of a pharmaceutically acceptable salt or physiologically functional derivative and a pharmaceutically acceptable diluent or carrier.
- 5 4. A compound according to claim 1 for the use as a medicament.

10

15

20

- 5. A method of treatment of a disease or a therapeutic indication in which inhibition of dihydrogratate dehydrogenase is beneficial comprising administering to a mammal an effective amount of a compound as defined in claim 1 or a physiologically functional derivative or a pharmacologically tolerable salt thereof.
- 6. The method of claim 5 wherein the disease or indication is selected from the group consisting of rheumatism, acute immunological disorders, autoimmune diseases, diseases caused by malignant cell proliferation, inflammatory diseases, diseases that are caused by protozoa infestations in humans and animals, diseases that are caused by viral infections and *Pneumocystis carinii*, fibrosis, uveitis, rhinitis, asthma and athropathy.
- 7. The use of a compound as defined in claim 1 for the inhibition of DHODH.
- 8. A process for the preparation of a compound as defined in claim 1.